

REMARKS

This is in response to the Examiner's Office Action mailed on November 19, 2003, Office Communication mailed on June 7, 2004 and Applicants' telephone conference with Examiner Patrick Lewis, Ph.D., on June 24, 2004. Claims 1-44 and 55 have been canceled. Claims 45 and 56 are amended. Claims 45-54 and 56 are pending in the application.

The Office Communication mailed on June 7, 2004 states that Applicants' reply filed on March 19, 2004 is not fully responsive to the Office Action mailed on November 19, 2003 because claims have been amended to read upon a non-elected invention. On June 24, 2004 Applicants had a telephone conference with Examiner Lewis who made an effort to ascertain that the statutory due date for our response to the Office Communication falls on July 7, 2004 and an extension of time is obtainable under 37 CFR 1.136(a).

In response to the Office Communication Applicants amend independent claim 45 to specify a method for preventing or reducing the risk of developing graft-versus-host disease (GVHD) in a patient who is a recipient of an organ or tissue transplant. The method includes the step of administering to the transplant recipient pentostatin in a pharmaceutically effective amount within a predetermined time window before the transplantation. Claim 45 as amended reads upon the elected invention drawn to a method for preventing or reducing the risk of developing GVHD.

In the Examiner's Office Action mailed on November 19, 2003, Claims 19, 21-22, 25-27 and 31-33 are rejected under 35 U.S.C. §112, first paragraph as failing to comply with the enablement requirement. Specifically, the Examiner states that there is limited predictability in the art that pentostatin is able to prevent GVHD wherein pentostatin is administered after surgery [transplantation]. The Examiner further requires Applicants to provide evidence that a population of individuals was treated with pentostatin after surgery and that population did not develop GVHD.

Applicants submit herewith an article published by Miller et al (2004) who conducted a clinical study of 55 patients who received hematopoietic stem cell transplant (HSCT) by using a regimen comprising pentostatin. Miller et al (2004) "A novel reduced intensity regimen for allogeneic hematopoietic stem cell transplantation associated with a reduced incidence of graft-versus-host disease" *Bone Marrow Transplantation* (2004) 33:881-889. As summarized in the Abstract of the article, the 55 patients at high risk or illegible for conventional HSCT received a

regimen consisting of extracorporeal photopheresis, pentostatin, and reduced dose total body irradiation. The study showed that the treatment was well tolerated and associated with a low incidence of transplant-related mortality and acute GVHD (aGVHD).

In the study, pentostatin was administered at a dose of 4 mg/m²/day by a continuous intravenous infusion for 2 consecutive days (days -5 and -4 before the transplantation). Page 883, column 1, 2nd paragraph, lines 1-3. The results showed that the regimen was associated with a lower than expected incidence of serious aGVHD and cGVHD (chronic GVHD). Compared to other regimens using purine analogs and low doses of TBI or melphalan which resulted in the incidence of aGVHD ranging from 25 to 50%, using the regimen including pentostatin only resulted in 9% incidence of grade II-IV aGVHD. Page 887, column 1, 3rd paragraph, lines 1-6. Further, the incidence of infection, complications, mixed chimerism, and disease relapse is low compared to the T-cell modified transplants. Page 887, column 1, 3rd paragraph, lines 9-11.

In view of Applicants' enabling teaching in the specification which is further supported by the clinical evidence showing the efficacy of pentostatin in preventing or reducing the risk of developing GVHD in patients, Applicants submit that the instant application has enabled one of ordinary skill in the art to make, use and practice the claimed invention under 35 U.S.C. §112, first paragraph. Withdrawal of the rejection is therefore respectfully requested.

Application No. 09/976,468
Supplemental Amendment dated: June 28, 2004
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CONCLUSION

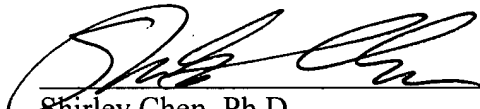
In light of the remarks and arguments set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

WILSON SONSINI GOODRICH & ROSATI

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By:



Shirley Chen, Ph.D.

Registration No. 44,608

650 Page Mill Road
Palo Alto, CA 94304-1050
(650) 565-3856
Client No. 021971